

THE LATE NODULAR SYPHILIDE

By DOUGLASS W. MONTGOMERY, M. D.

DISCUSSION by Harry E. Alderson, San Francisco; Anstruther Davidson, Los Angeles; Thomas J. Clark, Oakland.

Stigma monumenti revocans in memoriam iniquitatem, a memorial stigma bringing iniquity to remembrance.

The efficiency of the Wassermann reaction in detecting the presence of syphilis, and the success of arsphenamine in clearing up luetic lesions of the skin and mucous membranes is so marked that the importance of the clinical diagnosis of these interesting manifestations would seem to be diminished. Numerically this is so, as between 80 and 90 per cent of those afflicted with late lesions of the skin give a positive reaction. *The very success of the Wassermann reaction, however, makes it all the more desirable to be able to make the diagnosis clinically when it fails.* In practice we find it more and more frequent for both the physician and the patient to rely unqualifiedly on the laboratory diagnosis, which is a great evil.

Not long ago we had a patient with late active lues in the nose, in the roof of the mouth, and in a toe, and yet her serum reaction was negative. As practicing physicians we all are aware of the moral value of a positive, unshakable diagnosis as a support in carrying out an efficient, continuous line of treatment, and this support may be obtained equally well from the clinical manifestations as from the laboratory findings.

Then there are cases in which the patient may suffer from two different lesions, and it becomes eminently desirable to be able to say that one of these will heal expeditiously under the treatment, while the other will not do so.

There is still another weighty reason for rehearsing the clinical features of the late syphilides at every convenient opportunity. The success of arsphenamine in clearing up the lesions of the skin and mucous membranes, or in preventing their appearance, is so great that the occasions for seeing them have become quite infrequent. Even in large clinics teachers complain of the paucity of material for demonstration. It is therefore desirable to make the best use of the few chances available, and one can only do so by being prepared for the event.

The late nodular syphilide used to be called the tubercular syphilide because it was usually larger than the early papule and more sluggish in its course, but since so many nodular cutaneous affections have been recognized as appertaining to tuberculosis, the epithet "tubercular" has been dropped from the spirochetal affections entirely, as leading to confusion.

The late syphilitic papule, or nodule, both anatomically and etiologically, is the same as the early papule of the widespread papular or papulopustular rash. I well remember how surprised I was in sectioning a papule from a patient with a rare early miliary syphilide in the old Polyclinic to find that anatomically it was a minute gumma, even to the presence of giant cells, and a gumma is nothing more than a large, deeply situated, solitary nodule.

The greatest incidence of the late nodular syphilide is about the third year of the disease, but it may

occur even in the first year, and it has been known to appear as late as fifty-five years after the primary lesion (Fournier).

The nodule of syphilis is a little tumor, and this should always be borne in mind in considering a diagnosis. It is generally about the size of a small pea, and it has the substantiality of a tumor, both to the eye and to the finger. It looks to be, and really is, well set in the true skin, and may extend below it into the subcutaneous tissue. Its surface may be intact, rounded and smooth, and its characteristic color is deep red or that of raw ham, but it may be bright red. If it occurs as one sole lump or nodule, or a few such widely scattered, I do not know how to make the diagnosis clinically, but it seldom so occurs, except as a very large node, when it tends to central liquefaction and on opening discharges a glairy pus, and is called a gumma. Even here the resemblance between a syphilitic gumma and a tubercular gumma may be too close to differentiate. The course of the tubercular lesion is usually slower than that of syphilis, and the infiltration is usually softer. We have such a case under observation at present. The late nodular syphilide usually occurs as one of a group, and then its characteristics may be so distinctive that any well-trained physician may make the diagnosis. Like everything organic the luetic nodule grows to a size limited by its nature and then recedes.

The nodules of any group are all of different ages and therefore of different sizes, and their general appearance also differs with their age. An individual nodule may pass through its whole life cycle in or under a superficially intact skin, or possibly only give rise to some desquamation as an evidence of its inflammatory nature, and may disappear, leaving no surface evidence of its previous existence, or it may cause a scar. The presence of these scars in a nodular patch is of great diagnostic value. Individual nodules will almost certainly liquefy in the center, and in opening on the surface give rise to small steep-edged ulcers with a dirty grey base.

Instead of appearing as individual papules the late nodular syphilide may develop as a solid, continuous infiltration with a smooth, even surface and a definite border, just as tuberculosis may develop as an infiltration instead of separate tubercles. This type is rare, however.

THE ARRANGEMENT OF THE PAPULES

Notation of the arrangement of the papules is often most important, as on it may depend the diagnosis.

In contrast to the early papular eruption, which is bilateral as becomes a disease scattered universally by the blood current, the late nodular eruption often shows decided bilateral asymmetry.

We have before spoken of grouping as another peculiarity of diagnostic value, but the papules in the bunch may be numerous and well set apart, and may exhibit no arrangement whatever, constituting what may be called a "buckshot group." Many of the papules may break down into small circular steep-edged ulcers, some of which may be covered either with a yellow or with a black tightly adherent crust, while others will have healed, leaving white or



Circular ulcer of late syphilis. A band of epithelialization may be seen extending from about 5 o'clock on the circle toward the central nub, which will presently transform the circular ulcer into a kidney-shaped one.

reddish brown scars. The variegated appearance of the field may be imagined.

A nodular syphilide may begin as a single nodule, and then others may arise immediately around it, so spreading out continuously from the original center. The spread, however, does not usually take place in an even circle; only a segment remains active, forming an advancing wall, invading the normal skin. Ulceration follows the wall, so that a crescentic lesion is formed with an advancing bow-shaped indurated wall, within which there is a crescent-shaped ulcer, in the hollow of which there is scar tissue. This is the typical syphilitic horseshoe-shaped ulcer with the indurated border of raw ham color. This is the lesion so often mistaken for either lupus or epithelioma, but which is so much more rapid in its course than either of them.

In the development of such a patch quite a variety of grotesque figures may be formed. For instance, Gougerot recently showed a photograph in which two bows joined, forming the letter "S," as if the disease were trying to write its own signature, and recently I saw a crescentic ulcer in which the two horns of the crescent had met, forming a circular ulcer with a nub of sound skin in the center. Subsequently the healing began at one point on the edge and extended toward the central nub, as may be seen in the photograph. This circular ulcer will presently, therefore, again become a crescent-shaped one.

THE SITUATION OF THE LATE NODULAR SYPHILIDE

These syphilides have their favorite situations, and in their order of frequency they occur on the face,

especially on the wings of the nose, about the mouth, and on the forehead. On the forehead they may occur along the hair line, causing the corona veneris of the tertiary period. Next in frequency of location comes the palmar and plantar surfaces, the thighs, nape of the neck, posterior surface of the forearms, and the scapular and lumbar regions of the back. They may occur on any part of the cutaneous surface, but it is apparent from the above that the trained observer will pay particular attention to any destructive lesion about the nares, mouth or forehead, to see if by chance any additional signs of syphilis may be discovered.

SUPERINFECTION AND CRUSTING

The tissue of a late syphilitic nodule is diseased and of low resistance, and it is situated near the surface, and therefore is readily attacked by pyogenic bacteria. Under these conditions desquamation, ulceration and crusting are natural consequences.

THE ULCER RESULTING FROM THE SOLITARY NODULE

The solitary nodule may break down into an ulcer with a definite indurated border, on the surface of which the pus tends to dry, forming a crust. The spirochete is strongly inclined to attack the blood vessels, and I suppose it is because of this that the pus is so frequently mixed with blood. The admixture of blood makes the crust dark brown or black, and very tough. It is also very adherent and fits within the border of the ulcer like a watch crystal in its setting. As the ulcer extends the crust becomes larger, and at the same time rises above its base, and so takes on a roughly pyramidal shape, resembling an oyster shell. The indurated border and the black tightly adherent, accurately fitting, thick, rough pyramidal crust form a striking and characteristic picture.

THE DESQUAMATION AND CRUSTING OF THE GROUPED NODULAR SYPHILIDE

The nodules, as before remarked, may be grouped, but irregularly scattered. They may, however, be closely agglomerated so as to form a continuous desquamating surface, in which case the diagnosis may be impossible to make. I remember well an incident in the old Toland Clinic at North Beach that made a great impression upon me. A woman had what appeared to be an indurated eczema on the side of the nose near the eye, for which I prescribed ammoniated mercury ointment. At the next visit, a week later, the lesion had so cleared up as to show plainly its nodular character, and then I discovered several other stigmata of lues that had previously escaped my notice. It was a good illustration of the clinic axiom that one finds what one looks for.

The crusting may be impetiginous, and so thick as to completely hide the subjacent definite luetic symptoms, and so give rise to an erroneous diagnosis of impetiginous eczema, or of impetigo. In any doubtful case nodules and scars should be sought for.

One must also remember that it is impossible to tell beforehand how much real loss of substance has taken place under a crusted syphilide, and it is often

advisable to warn a patient of this, lest he blame the treatment for the deformity.

CONDYLOMA LATUM

When luetic papules occur on approximated surfaces of the skin or mucous tracts where they are kept warm and moist as in the vagina, between the labia, and in fat people in the groins and in the axillae they assume a different aspect.

They are steep-edged elevations, flattened on top, and are called condylomata lata, or flat venereal warts, in contradistinction to the condylomata acuminata, or pointed warts, with which they may be associated but which have a different etiology.

Condylomata lata usually occur in early constitutional syphilis, and used to be frequently met with. Since the introduction of arsphenamine they are rarely seen, and with their disappearance has gone the greatest danger of infection.

It is important to notice that here again we have a solid, broad, substantial lesion such as is so frequently found in syphilis.

The acuminate wart may arise from any irritating discharge, such as gonorrhea, or that from pyogenic bacteria, and are therefore frequently adventitious to the broad luetic warts. Because the acuminate warts so frequently owe their origin to the irritation of gonorrheal discharges, or to streptococcal infection on a luetic base, many associate them obligatorily with venereal disease. It is very especially worth noting, however, that they may occur on the privates during pregnancy without any venereal disease whatever. Years ago I saw with Dudley Tait a patient who, being pregnant, had nonvenereal acuminate warts of the genitalia. An injudicious practitioner had previously seen the patient, and had designated them as being venereal, with what might have been the most deplorable consequences.

SCARS FROM THE LATE PAPULAR SYPHILIDE

Scars following this form of syphilide are often characteristic. When recent they are frequently maculated reddish brown, because of the blood pigment they contain, a result of blood extravasation due to spirochetal injury to the blood vessels. For the same reason they may be bordered in brown. This brown pigmentation is most frequent and most persistent in lesions of the legs, especially of the lower third. After a time the scars become smooth, pliable, and white. Of course, scars are almost always unilateral, and solitary or grouped. A group of ulcers may become confluent and the resultant scar may be quite large, and have a polycyclic border, following in this respect the outer contours of the component ulcers.

A unilateral group of small scars on the forehead, or to one side of the vertebral column, or to one side of the sternum may be due, not to syphilis, but to herpes zoster.

In regard to scars of the leg, those of the lower third may be ascribed to *ulcus cruris*, but those of the upper third, and especially about the knee, when not due to traumatism, are strongly suggestive of lues.

Enough has been said to indicate how many different clinical pictures may be produced by the differences in behavior of the purely spirochetal lesions themselves, and then add to these the differences pro-

duced by the superinfections, and those due to the constitution of the patient affected. It would be impossible to enumerate them. Often in descriptive work one has to take up the parts of a picture, frequently to utterly fail to convey the picture as a whole. The only way to keep the parts together in clinical pictures exhibiting such a variety is to constantly recur to the well-known pathology of syphilis and to the symptoms we know to be produced by the spirochete in the tissues, and these are the solidity of the infiltration, the prominence of the lesions, the tendency to grouping, the often concentric advance and fairly rapid progress, the painlessness, the ulceration, and the scarring.

DISCUSSION

HARRY E. ALDERSON, M. D. (490 Post Street, San Francisco)—Doctor Montgomery in his usual interesting and instructive manner has called attention to the clinical diagnostic features of nodular syphilides. He mentions the very great importance of not neglecting the clinical side of dermatology. Our present laboratory aids are indispensable, but the same may be said of our clinical observations. To depend blindly upon the laboratory or clinical findings alone is a serious mistake.

Typical nodules (or gummata) of this type are, to the experienced physician, diagnostic of lues. We frequently begin treatment of these patients while awaiting the result of the Wassermann and never have failed to see our diagnosis confirmed either serologically or therapeutically. We are indebted to Doctor Montgomery for this timely appeal and interesting description of a type of luetic skin lesion that all should be familiar with.

ANSTRUTHER DAVIDSON, M. D. (419 South Alvarado Street, Los Angeles)—Doctor Montgomery has emphasized the necessity for accurate clinical diagnosis of nodular lesions in those ulcerations that are Wassermann negative or weakly positive. In such cases, to determine whether lesions around the nostrils are syphilitic or cancerous, is difficult and the diagnosis is wholly dependent on those features the author so clearly points out. There is little room for discussion on a paper on the contents of which we are all in agreement. I would like to add that while the scarring produced by a nodular syphilide is very characteristic, it is almost impossible at times to differentiate it from those produced by blastomycosis or the superficial form of sporotrichosis.

THOMAS J. CLARK, M. D. (Oakland Bank Building, Oakland)—Doctor Montgomery in his interesting review of the salient points of nodular lues stresses some capital reasons for close observation of skin lesions so that the physician may strengthen his diagnostic acumen.

Doctor Montgomery's training was in the school where observation, comparison, careful analysis of the course of events, and the search microscopically for the minute structure of lesions was the evidence to be secured to warrant his diagnosis. This habit of thought in gathering clinical points does give results. We feel assurance to have a master say, this is lues, or epithelioma or lupus.

Careful habits of search for clinical evidence is the school producing such men as William Osler.

It is interesting to see the persistence of syphilis and we do well to keep our judgment balanced about this feature. It is easy to ascribe all obscure pathology to syphilis. If we remember, the course of the disease is so well defined in the majority of cases it gave rise to the clinical arrangement of primary, secondary and tertiary periods, these different periods showing a rather acute local process of inflammation, followed by a widely distributed or generalized inflammatory reaction which gradually subsided to a local disturbance in the tissues. Montgomery calls our attention to these features of the tertiary nodulation—color, asymmetry of distribution, lack of pain, scarring, and a more rapid course than that of lupus or epithelioma.

The percentage of successful diagnosis of syphilis is highest during the secondary or generalized stage. This is followed by more or less active treatment. With the

tertiary lesions the percentage of positive blood findings drops sharply, so it is very important to recognize the disease by its clinical characteristics.

Doctor Montgomery's broadminded attitude of using these cases of tertiary syphilis to educate the younger medical men is commendable.

QUANTITATIVE ESTIMATION OF ALBUMIN IN URINE

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San Francisco)

THIS paper relates the details of an accurate and rapid method for the quantitative estimation of albumin in urine. The discussion is limited, first, to a brief review of the inaccuracy and delays encountered in using the ordinary textbook procedures and, second, to the technical aspect of the test, without any consideration of the pathological significance of albuminuria.

In February, 1925, a patient in whom we were especially interested developed an albuminuria of such a high degree that it was impossible to obtain a reading on the Esbach tube without diluting the original specimen. This was done with water, although most textbooks simply state "to dilute," but do not specify the diluent. Our readings seemed somewhat large, so we set up a series of dilutions and found that as the dilution increased we obtained greater estimations of albumin. The results when compared with gravimetric determination on the same specimens proved the inaccuracy of diluting urine with water. Those interested in laboratory analyses are aware of the fact that the Esbach determination of albumin in urine gives only an approximate estimation, requires twenty-four hours' time, and is influenced by many factors, yet it is probably the most widely used method.

Since we now know that diluting urine with water increased the inaccuracy of albumin determinations by the Esbach test, and since we did not think that the gravimetric or other known accurate quantitative methods were practical as routine procedures, we set out to find something which could be relied on to dilute urine without disproportionately altering the albumin content.

Many fluids were tried, including the following: Albumin free urine, Tsuchya's reagent, 2 per cent acetic acid, various strengths of alcohol, sodium chloride solutions (2 per cent to .85 per cent), and others. In brief, all the above solutions as diluting fluids were found to yield inaccurate results. Tsuchya's reagent or alcohol used as diluting fluids decreased disproportionately the albumin estimation. Beginning with 2 per cent sodium chloride and decreasing to a concentration of .85 per cent, inaccurate results were obtained similar to those when water was used as diluent. We noted, however, that 2 per cent sodium chloride yielded results which were more promising.

At this point in our work we discovered that Doctor Wykoff of Stanford University Hospital was working independently on the same problem, and that he began at 2 per cent sodium chloride and, working with increasing concentrations, found that 2.5 per cent sodium chloride was the desired strength to be used. He was also working with a standard

control of egg albumin, using a modified Purdy technique for the test.

With these facts we now felt that our difficulties were about over, but believed that a standard made from human blood serum would perhaps be more nearly ideal, since urinary albumin so closely resembles the coagulable proteins in the blood serum. Then, too, Folin, in his laboratory manual, gives the details of a test, using a standard made with hemoglobin free sheep's blood serum, so you see the idea is not new. Sheep's blood serum is not as readily obtained in our laboratory as is human serum, so it seemed quite logical to use the latter as a standard.

It was found that 5 mls. of pooled human serums diluted to 100 mls. with 2.5 per cent sodium chloride solution yielded by gravimetric determination an average albumin content of 6 grams per liter. With this standard solution we then proceeded to shorten the time element from twenty-four hours to fifteen minutes by adopting a modified Purdy test instead of the Esbach.

The procedure as now used is as follows: Place in a 15 mls. capacity graduated centrifuge tube 10 mls. of urine to be tested, and in another similar tube 10 mls. of standard serum solution; then add to each tube 5 mls. of Tsuchya's reagent (phosphotungstic acid 15 gms. hydrochloric acid 50 mls., and make up to 1000 mls. with alcohol 95 per cent); mix thoroughly by inverting back and forth, and let stand for ten minutes; then place the tubes in the centrifuge and centrifugalize for three to five minutes. Record the amount of precipitate in each tube and calculate the result.*

The standard tube reading equals 6 gms. albumin per liter.

We have made over one thousand determinations, using the above technique as routine, with frequent checks by the gravimetric method. The average difference was 3 per cent higher by the centrifuge method. In many determinations identical results were obtained, figuring to one decimal. No attempt has been made to estimate closer with one decigram. Slight errors may readily occur in reading amounts between the graduations on the centrifuge tube, and also in the gravimetric method, if the sediment is not properly dried to a constant weight.

When using the above method it must be remembered that the standard is set up at the same time as the unknown, and that all solutions are kept under the same temperature conditions at all times until the final reading is made. In this way only is one justified in comparing results. If it is necessary to dilute the unknown, do so with 2.5 per cent sodium chloride solution, a stock bottle of which is kept under the same temperature conditions as the standard and unknown. In this laboratory it has been practical to keep our standard solutions at room temperature.

The standard solution is made fresh each week, oftener only when the stock has been used. A small amount of preservative (chloroform 1 to 1.5 mls. per 100 mls. of serum solution) can be added to prevent bacterial growth or other determination. In

* The supernatant fluid should be water clear after centrifuging. If there is the slightest turbidity then the concentration of albumin is too great for complete precipitation, and the original specimen must be diluted. This necessitates repeating the entire procedure.